

Clinical manifestations, management, and outcomes of primary silent sinus syndrome: a systematic review*

Lauren Michelle, Amy T. Du, Arash Abiri, Edward C. Kuan

Department of Otolaryngology - Head and Neck Surgery, University of California Irvine Medical Center, Orange, CA, USA

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Abstract

Introduction: Silent sinus syndrome (SSS) is a rare disorder of the maxillary sinus, which may present with orbital symptoms. Most reports of silent sinus syndrome are limited to small series or case reports. This systematic review comprehensively characterizes the various clinical presentations, management, treatment, and outcomes in patients with SSS.

Methods: A systematic literature search of the PubMed, Cochrane, Web of Science, and Scopus databases. Inclusion criteria were studies describing the presentation, management, or treatment of SSS or chronic maxillary atelectasis.

Results: One hundred fifty-three articles were included in the final review (n=558 patients). Mean age at diagnosis was 38.8 ± 14.1 years, with a relatively even distribution among sexes. Enophthalmos and/or hypoglobus were the most frequent symptoms, along with diplopia, headache, or facial pressure/pain. Most patients (87%) underwent functional endoscopic sinus surgery (FESS), and 23.5% received orbital floor reconstruction. Post-treatment, patients had significant reductions in enophthalmos (2.67 ± 1.39 vs. 0.33 ± 0.75 mm) and hypoglobus (2.22 ± 1.43 vs. 0.23 ± 0.62 mm). Most patients (83.2%) achieved partial or total resolution of clinical symptoms.

Conclusions: SSS has a variable clinical presentation, with enophthalmos and hypoglobus being most common. FESS with or without orbital reconstruction are effective treatments to address the underlying pathology and structural deficits.

Key words: chronic maxillary atelectasis, imploding antrum, silent sinus syndrome, spontaneous enophthalmos, spontaneous hypoglobus

Introduction

Silent sinus syndrome (SSS), also known as imploding antrum syndrome or spontaneous enophthalmos, is the result of chronic maxillary sinus atelectasis and remodeling of the orbital floor⁽¹⁾. Clinically, patients typically present between 30-60 years old with a progressive but painless ipsilateral enophthalmos and/or hypoglobus, with partial or total opacification of the maxillary sinus⁽²⁾. It is difficult to accurately estimate incidence or prevalence of SSS given its rarity, and most reports in the literature have been limited to case reports and case series published in the ophthalmology, otolaryngology, and radiology literature. While the syndrome was described in the literature as early as 1981 by Wilkins and colleagues, the term "silent sinus syndrome" was first used by Soparkar et al in a 1994 multicenter retrospec-

tive review of 19 cases^(3,4). The authors concluded that the above constellation of clinical findings in the absence of trauma or surgery represented a new syndrome previously undescribed⁽³⁾. Initially thought to be due to a preexisting hypoplasia of the maxillary sinus, further case reports have since established the presence of patients with normal sinus anatomy on imaging prior to developing SSS⁽⁵⁾. Understanding of the pathophysiology of SSS has since evolved, and is now known to be primarily driven by obstruction of the osteomeatal complex, development of hypoventilation and negative pressure of the maxillary sinus, and subsequent collapse of the sinus with inward bowing of the ipsilateral orbital floor⁽⁵⁻⁷⁾. Management involves restoring healthy maxillary sinus ventilation and anatomy and may also require simultaneous or

asynchronous repair of the orbital floor. Prior accounts of SSS have largely been limited to case series and reports. This systematic review of the literature comprehensively analyzes existing reports of SSS and discusses the various clinical presentations and current strategies in management.

Materials and methods

This systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. Because deidentified data from existing published literature databases was utilized, no Institutional Review Board approval was required.

Search strategy

A comprehensive search was performed in PubMed (1975-2021), Cochrane (2013-2020), Web of Science (1981-2021), and Scopus (1981-2022) databases in June 2022 using key words "silent sinus syndrome" OR "chronic maxillary atelectasis" OR "impinging antrum" OR "spontaneous enophthalmos" OR "spontaneous hypoglobus". Articles were initially screened via Covidence v2708 by title name and abstract contents by two independent investigators (L.M. and A.D.) using inclusion and exclusion criteria. Conflicts in article interpretation were resolved by the senior author (E.C.K.). Full text articles were then reviewed for final incorporation into the systematic review.

Selection criteria, data extraction, and statistical analysis

Inclusion criteria were clinical studies or case reports describing or characterizing the presentation, management, or treatment of silent sinus syndrome or chronic maxillary atelectasis (CMA) in patients of any age. Exclusion criteria were as follows: 1) reports involving history of facial trauma or previous sinus surgery, 2) studies which described CMA stage I or stage II only, 3) studies lacking primary data (e.g., reviews, comments, meta-analyses, letters to the editor). Risk of bias of individual studies was assessed by assigning articles "Levels of Evidence" scores developed by the Oxford Centre for Evidence-Based Medicine⁽⁸⁾. All information on patient age, sex, clinical and radiological presentation, SSS laterality, treatments, outcomes, and adverse events were extracted and processed in IBM SPSS v.28.0.0.0 (Armonk, NY, USA). Wilcoxon rank sum tests were used to evaluate intra-patient differences in the means of continuous variables. A p-value of <0.05 was considered statistically significant.

Results

Database searching yielded 246 results from PubMed, 280 articles from Web of Science, 239 studies from Scopus, and 3 results from Cochrane. Search results yielded 298 unduplicated results, and 153 articles were included in the final review (Figure 1). A total of 558 patients were included across 1 prospective non-randomized clinical study, 28 retrospective studies, and 124

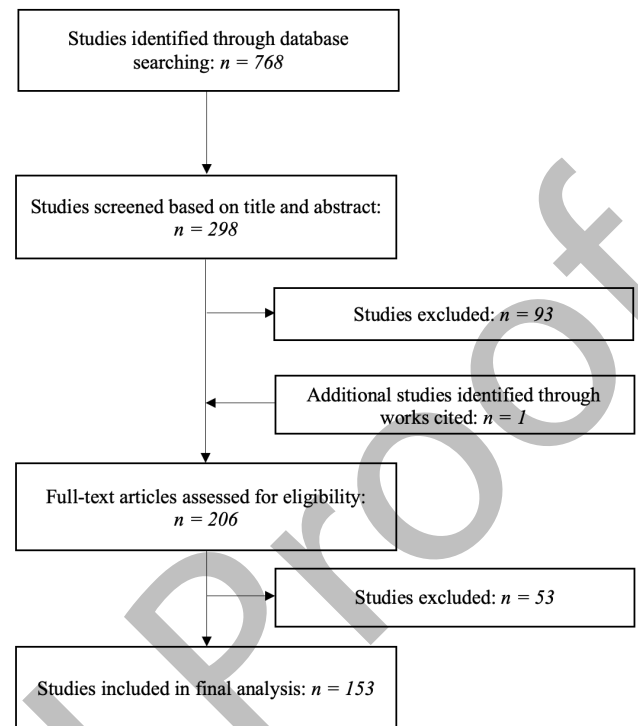


Figure 1. Flow chart depicting PRISMA search for studies on the characterization, presentation, and management of silent sinus syndrome.

case reports or case series (Table 1). Studies with single-subject data are summarized in Table 2.

Among the included cases, the mean age at diagnosis was 38.8 ± 14.1 years (range, 7-76 years, median 39.0). There were 221 female (39.6%) and 246 (44.1%) male patients, with 91 (16.3%) patients whose sex was undisclosed. SSS affected 218 (39.1%) patients on the right side, 173 (31.0%) patients on the left side, 14 (2.5%) patients bilaterally, and 153 (27.4%) patients with unreported laterality. Mean reported follow-up (n=71 studies) was $14.8 \text{ months} \pm 18.9 \text{ months}$.

The most common presenting symptoms were enophthalmos (280/354, mean $2.67 \pm 1.39 \text{ mm}$) and/or hypoglobus (183/257, mean $2.22 \pm 1.43 \text{ mm}$), with a minority of patients experiencing diplopia (n=78/215), headache (n=19/271), or facial pressure/pain (n=85/290). In the 364 cases where computed tomography (CT) scan results were reported, 67 (18.4%) patients had complete and 26 (7.1%) had partial opacification of the affected sinus. Degree of opacification was not specified in 147 (40.4%) cases. Collapse, retraction, atelectasis, or hypoplasia of at least one wall of the affected sinus was reported in 309/339 cases, most commonly with downward bowing of the orbital floor forming the roof of the maxillary sinus. Rarely, cases of frontal (n=1) or ethmoid (n=3) SSS were reported (9-12).

In cases where treatment was described (n=426), the therapy of choice for the majority of patients (n=371) was functional

Table 1. Summary of search results on the presentation and management of silent sinus syndrome.

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Follow up (months)	Adverse Events
Wilkins, 1981 ⁴	5	-	-	EOT, HG	-	-	-	-	-	-
Wesley, 1986 ²⁵	1	27	F	EOT	SA	L	CL, OFR	Minimal residual enophthalmos	30	none
So, 1994 ²²	19	36 mean (29-46 range)	-	EOT, HG	SA	-	-	-	-	-
Dailey, 1995 ²⁶	2	35-42 range	1F, 1M	EOT, HG, lagophthalmos	SA	2R	CL, OFR	RS	12	none
Kass, 1996 ⁷	2	33-41 range	1F, 1M	HG	-	-	FESS	Stable	6	none
Kass, 1997 ²¹	5	33-45 range	F	EOT, HG	SA, SO	2R, 3L	FESS, CL	RS	6	none
Durig, 1998 ²⁷	1	55	M	EOT, HG, DP	Thinned orbital floor, maxillary sinus mucocele	2L	FESS, OFR	RS	-	none
Gillman, 1999 ²⁸	2	44-47 range	1F, 1M	EOT	SA, SO	1R, 1L	FESS, septoplasty	Stable	12	none
Davidson, 1999 ⁵	1	27	F	EOT, HG	SA, SO	R	FESS, OFR	-	-	none
Wan, 2000 ²⁹	3	38-44 range	1F, 2M	EOT, HG	SA, SO, septal deviation	1R, 1L, 1BL	FESS	RS	-	none
Kubis, 2000 ³⁰	1	32	F	EOT, change in palpebral fissure	SA, SO	L	FESS, OFR	RS	18	Mild, transient vertical diplopia which resolved
Hunt, 2000 ³¹	1	49	M	EOT, HG, change in palpebral fissure	SA, SO	L	FESS	RS	6	Symptomatic L frontal sinusitis unresponsive to medical therapy
Raghavan, 2001 ³²	1	29	M	HG	SA, SO	R	FESS, OFR	RS	36	none
Vander Meer, 2001 ²³	4	38-47 range	1F, 2M	EOT, HG, FP	SA, SO	2R, 2L	FESS, OFR	RS	10	none
Illner, 2002 ³³	5	47 mean (39-65 range)	1F, 4M	EOT, HG, DP, FP	SA, SO	3R, 2L	FESS	-	-	-
Castelein, 2002 ³⁴	1	-	-	EOT	-	-	FESS	RS	-	-
Ende, 2002 ³⁵	1	32	F	HG, DP	SA, SO	L	FESS	Stable	40	none
Audemard, 2002 ³⁶	1	29	F	EOT, DP, FP	SR	L	FESS	RS	-	-
Thomas, 2003 ³⁷	4	27-40 range	2F, 2M	HG	SA, SO	2R, 2L	FESS, OFR, septoplasty	RS	6	none

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
Rose, 2003 ³⁸	14	41.3 mean (25-78 range)	7F, 7M	EOT, HG, DP, FP	SA, SO, increased fat in PPG fossa	8R, 6L	FESS, OFR	RS	4-33 mo	-
Yip, 2003 ³⁹	1	9	F	EOT, HG, DP	SA, SO	R	-	-	-	-
Roach, 2003 ⁴⁰	1	28	F	EOT	SA, SO	R	-	-	-	-
Ong, 2003 ⁴¹	1	46	F	HG	SA, SO	L	FESS	RS	-	-
Iseli, 2003 ⁴²	1	56	M	EOT, HG, DP	SA	L	Prisms for diplopia	Stable	22	none
Wang, 2004 ⁴³	1	75	M	EOT, HG, DP	SA, SO	L	-	-	-	-
Hobbs, 2004 ⁴⁴	1	27	F	EOT, HG	SA, SO	L	FESS, septo-plasty	RS	-	none
Hira, 2004 ⁴⁵	1	28	F	EOT, HG	SA, SO	L	FESS, OFR	RS	2	none
Hobbs, 2004 ⁴⁶	1	41	F	EOT, DP, FP	SO	R	FESS	RS	-	-
Rapidis, 2004 ⁴⁷	2	32-36 range	1F, 1M	EOT, HG, change in palpebral sulcus	SA	2L	CL, OFR	RS	36	none
Hens, 2005 ⁴⁸	2	25 mean	6F, 6M	EOT	-	-	FESS	-	-	-
Toh, 2005 ⁴⁹	1	29	F	FP, change in palpebral sulcus	SA, SO	R	FESS	-	-	-
Sonbolestan, 2005 ⁵⁰	1	58	F	EOT, FP	SA	R	Diagnostic nasal endoscopy	-	-	-
Braganza, 2005 ⁹	1	32	F	EOT, change in palpebral fissure	SA, SO	R	FESS	RS	6	none
Yiotakis, 2005 ⁵¹	1	33	M	EOT, HG	SA, SO	-	FESS	RS	12	none
Numa, 2005 ⁵²	1	33	M	EOT, HG, DP	SA, SO	R	FESS, OFR	RS	-	none
Ibanez Mico, 2005 ⁵³	1	14	F	EOT	SO	R	None	Stable	-	none
Ando, 2005 ⁵⁴	2	36-50 range	1F, 1M	EOT, HG, change in palpebral fissure	SO	1R, 1L	FESS, OFR	RS	-	none
Nkenke E, 2005 ⁵⁵	1	26	F	EOT, HG	SA, SO	R	FESS, OFR	RS	3	none
Hourany R, 2005 ⁵⁶	1	30	M	EOT, HG	SO	R	None	Stable	-	none
Behbehani, 2006 ¹⁵	5	32-42 range	3F, 2M	HG, change in eye size, contact lens falling out	SA, SO	2R, 3L	FESS, OFR	RS	-	none
Babinski, 2006 ⁵⁷	3	20-39 range	1F, 2M	EOT, DP	SA, SO	-	FESS, septo-plasty	Minimal residual enophthalmos	-	-
Kaeser, 2006 ⁵⁸	1	31	M	EOT, change in palpebral fissure	Sinusitis	R	FESS	Asymptomatic at 6 mo f/u	6	none
Facon, 2006 ⁵⁹	1	56	F	EOT, FP	SA	R	FESS	RS	2	none
Dinis, 2006 ⁶⁰	1	35	M	EOT	SO	L	FESS, OFR	RS	-	none
Wise, 2007 ⁶¹	11	46.5 mean	4F, 7M	EOT, DP, FP	SA, SO	-	FESS	-	-	none

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
Rodriguez, 2007 ⁶²	1	66	M	EOT	-	R	FESS, OFR	RS	3	none
Moreno, 2007 ⁶³	1	45	F	HG	SA, SO	R	FESS	RS	1	none
Burduk, 2007 ⁶⁴	1	15	M	Malar cheek depression	-	R	FESS	RS	-	none
Brochart, 2007 ⁶⁵	1	22	F	EOT	SO	L	CL, OFR	-	-	none
Vaidhyath, 2008 ⁶⁶	1	66	F	EOT	SO	R	FESS	RS	-	none
Sanchez-Dalmau, 2008 ⁶⁷	1	29	F	EOT, HG	SA	R	FESS	RS	-	none
Gomez, 2008 ⁶⁸	1	59	M	EOT	SO	L	FESS, OFR	RS	6	none
Habibi, 2008 ⁶⁹	1	16	F	EOT	SA, SO	L	CL procedure, enucleation of large maxillary sinus mucocele	RS	24	none
Tan, 2008 ⁷⁰	1	21	M	EOT, HG, change in palpebral fissure	SA, SO	R	FESS, OFR	RS	-	none
Korn, 2009 ⁷¹	5	4 M, 1 F; 40.6 yo mean	4 M, 1 F; 40.6 yo mean	EOT, HG, change in palpebral fissure	-	-	FESS, OFR	RS	-	Transient hypoesthesia of midface (n=1)
Babin, 2009 ⁷²	18	19-54 range	14 F, 9 M	EOT, facial asymmetry	SA, SO	12R, 6L	FESS, septoplasty	RS, minimal residual enophthalmos	15	Persistent enophthalmos (n=1)
Miman, 2009 ⁷³	1	-	-	Existing SSS diagnosis	SA, SO	-	FESS	RS	8	none
Arikan, 2009 ⁷⁴	1	33	F	EOT, HG, change in palpebral fissure	SA	L	FESS, OFR	RS	3	none
Stevens, 2010 ⁷⁵	1	42	M	EOT, HG, DP	SA	L	OFR	RS	-	none
McArdle, 2010 ¹⁰	1	33	F	Change in palpebral sulcus, HA	SO	L	FESS	Minimal residual enophthalmos	-	none
Heilmeier, 2010 ⁷⁶	1	57	-	EOT	Imploded lamina papyracea	L	Blepharoplasty	-	-	none
AlonsterHoeven, 2010 ⁷⁷	1	57	M	HG, change in palpebral sulcus	SA, SO	R	CL	RS	12	none
Sesenna, 2010 ⁷⁸	3	28-46 range	1F, 2M	EOT, HG, DP, change in palpebral fissure	SA, SO	3L	FESS, OFR	RS	16	none
Waqar, 2010 ⁷⁹	1	27	M	EOT, HG	SA, SO	R	FESS	Minimal residual enophthalmos	2	none
Zhang, 2010 ⁸⁰	1	41	M	EOT, HG, DP	SA	R	Inferior oblique myectomy	RS	1.5	none
Babar-Craig, 2011 ⁸¹	16	-	-	-	-	-	FESS, intranasal steroids and decongestions	RS	31	none

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
George, 2011 ⁸²	1	28	F	EOT, HG	SA, SO	R	FESS	RS	6	none
Liss, 2011 ⁸³	1	56	M	EOT, HG, lagopthalmos	-	BL	FESS, OFR	RS	18	none
Haefliger, 2011 ⁸⁴	1	36	F	EOT, HG, change in palpebral fissure	SA, SO	R	FESS	Stable	18	none
Izadi, 2011 ⁸⁵	1	35	M	EOT	SA, obstructed nasolacrimal duct	L	Endoscopic washout	Biopsy showed non-caseating granulomas/sarcoidosis	-	none
Singh, 2011 ⁸⁶	1	44	M	EOT, HG	SA, SO	R	FESS	-	-	none
Mavrikakis, 2012 ⁸⁷	1	44	F	EOT, change in palpebral fissure	-	L	FESS, HAG injection	RS	6	none
Ferri, 2012 ⁸⁸	1	27	F	EOT, DP, change in palpebral fissure	SA	L	FESS, OFR	RS	1	none
Bas, 2012 ⁸⁹	1	27	M	EOT, HG	SA	R	-	-	-	-
Barbosa, 2012 ⁹⁰	2	34-65 range	2M	EOT	-	-	FESS	RS	-	-
Cobb, 2012 ⁹¹	1	42	M	DP, facial asymmetry	SA, SO	L	FESS, OFR, septoplasty	RS	36	none
Suh, 2012 ⁹²	1	29	M	-	SA	BL	FESS	-	-	none
Bahgat, 2012 ⁹³	1	35	M	HG, malar cheek depression	SA, SO	L	FESS	Stable	6	none
Bas, 2012 ⁸⁹	1	27	M	EOT, HG	SO	R	-	-	-	-
Gaudino, 2013 ⁹⁴	6	44 mean (22-67 range)	2F, 4M	EOT, HG, DP, facial asymmetry	SA, SO	2R, 4L	FESS, OFR	Stable	-	none
Kohn, 2013 ⁹⁵	22	22-70 range (mean 41.2)	8F, 14M	EOT, HG, septal deviation	SA, SO, increased fat in PPG fossa	14R, 7L	-	-	-	-
Sheikhi, 2013 ³²	1	60	F	EOT, facial asymmetry	SA, SO	R	-	-	-	-
Naik, 2013 ¹¹	1	48	M	EOT	SO due to obstructing type III Kuhn cell	L	FESS with removal of obstructing cell	RS	-	none
Saldanha, 2013 ⁹⁶	1	20	M	FP, malar cheek depression	SA, SO	R	FESS	Stable	3	none
Saffra, 2013 ⁹⁷	1	76	M	DP, FP	SA, SO	R	None	Stable	12	none
Grusha, 2013 ⁹⁸	1	43	F	EOT, HG	SA	-	FESS, HAG injection	RS	-	-
Guillen, 2013 ⁹⁹	1	66	M	HG	SA, SO	L	FESS	RS	-	none
Eisa, 2013 ¹⁰⁰	1	23	F	EOT, HG	SA, SO	L	FESS, OFR	RS	3	none
Singman, 2014 ¹⁰¹	1	39	M	DP	SA	L	FESS, OFR, septoplasty	RS with continued need for prisms	48	none

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
Van Meche- len, 2014 ¹⁰²	1	29	F	HA, nasal obstruc- tion	SO	R	FESS	-	-	-
Mohindra, 2014 ¹⁰³	1	12	F	EOT, HG, DP, eye asymmetry	SA	R	FESS, OFR	RS	8	none
Gomez, 2014 ¹⁰⁴	1	53	M	EOT, HG	SO, septal deviation	R	-	-	-	-
Fonseca, 2014 ¹⁰⁵	1	8	M	Extraocular mus- cle weakness	SA, SO	L	FESS	Stable	12	none
Kram, 2014 ¹⁰⁶	1	27	F	EOT, change in palpebral fissure	SA, SO	BL	FESS	Mild residual enophthal- mos	5	none
Kilty, 2014 ¹⁰⁷	1	40	F	FP	SO	R	FESS	RS	3	none
Chang, 2014 ¹⁰⁸	1	7	F	EOT, HG, facial asymmetry	SA, SO	R	FESS	RS	12	none
Gan, 2014 ¹⁰⁹	1	44	F	EOT, HG, nasal obstruction	SA, SO	L	FESS	RS	-	none
Savvateeva, 2015 ¹¹⁰	14	-	-	-	-	-	FESS	RS	-	-
Lin, 2015 ¹¹¹	22	44.6 mean	12F, 10M	EOT, DP, FP, septal deviation, nasal obstruction	SA	12R, 9L, 1BL	FESS, OFR	RS	11	none
Grusha, 2015 ¹¹²	1	45	F	EOT, HG	SA, SO	L	FESS, HAG injection	Stable, recurrence of minimal enophthal- mos with re-peat injection	18	none
Gomez, 2015 ¹¹³	1	53	F	EOT, DP	SA, SO	L	None	-	-	-
Gokmen, 2015 ¹¹⁴	1	35	M	HG, change in palpebral sulcus	SO	R	FESS	RS	-	none
Claros, 2015 ¹¹⁵	2	39-45	1F, 1M	EOT	SA	-	FESS, OFR	RS	-	none
Berczynski, 2015 ¹¹⁶	1	48	F	EOT, change in vision	SA	R	Removal of posterior nasal spine, OFR	-	-	none
Magalhães, 2015 ¹¹⁷	1	33	F	EOT, HG	SO	R	FESS	Mild residual enophthal- mos	-	none
Dumitrescu, 2015 ¹¹⁸	1	46	-	EOT, HG, DP, facial asymmetry	SA, SO	L	FESS	RS	-	none
Kashima, 2016 ¹¹⁹	11	39.5 mean (23-62 range)	1F, 10M	Orbital asymme- try, FP, DP	-	6R, 5L	Balloon sinus dilatation, OFR with cartilage	RS	7	Infectious sinusitis (n=1), 1 mm overcorrec- tion (n=1), lower eyelid retraction (n=1), naso- lacrimal duct obstruction (n=1)
Martínez- Capoccioni, 2016 ¹²⁰	20	43 mean (28-67 range)	14F, 6M	EOT, FP, nasal obstruction	SA, SO	12R, 8L	FESS, septo- plasty	Stable	5-18mo	none

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
Eyigör, 2016 ¹²¹	16	42.37 mean (20-66 range)	10F, 6M	EOT, HG, nasal obstruction	SA	8R, 8L	FESS or none	-	-	none
Kim, 2016 ¹²²	1	35	F	EOT, HG	SA, SO	R	FESS, blepha- roplasty	RS	-	none
Sen, 2016 ¹²³	1	17	M	Change in palpe- bral sulcus, FP	SA, SO	L	FESS	Stable	6	none
Ferro, 2016 ¹²⁴	1	28	F	FP	SA, SO	L	None	RS	-	-
Chavez- Montoya, 2017 ¹²⁵	3	37-48	1F, 2M	EOT, HG, DP, facial asymmetry, nasal obstruction	SA, SO	2R, 1L	FESS	RS	-	-
de Dorlo- dot, 2017 ²⁰	13	23-71 range	3F, 10M	EOT, DP, FP	SA, SO, septal deviation	10R, 3L	FESS	RS, minimal residual enophthal- mos, delayed OFR	6	none
Farneti, 2017 ¹²⁶	6	7-14 range	1F, 5M	EOT, HG, HA, sinusitis	SA, SO	3R, 3L	FESS	RS, minimal residual enophthal- mos, delayed OFR	71	none
Shieh, 2017 ¹²⁷	1	68	F	Thyroid eye disease with proptosis	SO	R	FESS	RS	1	-
Tieghi, 2017 ¹²⁸	1	43	F	EOT, HG, change in palebral sulcus, malar depression	SA, SO	R	FESS, OFR	RS	0.5	none
Trope, 2017 ¹²⁹	1	57	M	-	SO	L	FESS	Stable	-	-
Lau, 2017 ¹³⁰	1	59	M	Upper alveolar numbness	SA, SO	L	FESS	RS	4	none
Varas, 2017 ¹³¹	1	49	F	EOT, change in palpebral fissure	SA, SO	L	-	-	-	-
Kikuta 2017 ¹³²	1	40	F	DP, malar cheek depression	SA, SO	L	FESS	RS	12	none
Wang 2018 ¹³³	8	48.1 yo mean	-	EOT, HG, FP	SA, SO	4R, 4L	FESS	RS	-	none
Saito, 2018 ¹³⁴	1	-	-	-	Inverted papilloma of maxil- lary sinus	-	FESS	RS	-	none
Cohn, 2018 ¹³⁵	1	55	M	EOT, HG, DP	-	L	FESS, OFR	RS	-	none
Tribich, 2018 ¹³⁶	1	49	M	Facial paraesthe- sia, DP	SO	R	FESS	RS, prism lenses for diplopia	-	none
Reggie, 2018 ¹³⁷	1	32	F	Transient ipsila- teral monocular vision loss during intense laughter	SO	R	FESS	RS	7	none
Lee, 2018 ¹³⁸	3	37-55	3M	DP	SA	L	FESS	RS	-	-
Claros, 2019 ¹³⁹	15	25-53 range	11F, 4M	EOT, HG	SO	6R, 9L	FESS, OFR	RS	-	-

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
Nemet, 2019 ¹⁴⁰	5	-	-	Progressive enophthalmos and hypoglobus	SA	-	FESS, OFR	-	-	-
Jacobs, 2019 ¹⁴¹	1	47	M	EOT, DP	SA, SO	R	FESS	Persistence of diplopia	3	none
Weiss, 2019 ¹⁴²	1	38	F	EOT, HG, mild abducens nerve palsy	SA, SO	L	FESS	RS	1	none
Vahdani, 2019 ¹⁴³	1	40	M	EOT, HG	SO	BL	FESS, OFR	RS, later developed contralateral SSS	108	none
Bhalla, 2019 ¹⁴⁴	1	57	F	HG	SA	R	None	-	6	none
Arnon, 2019 ¹⁴⁵	1	30	M	EOT, HG, DP, facial asymmetry	SA, SO	R	FESS, OFR	RS	2	none
Hildenbrand, 2020 ¹⁴⁶	7	41 mean	-	EOT, maxillary pressure	SA, SO	3R, 3L, 1BL	FESS	RS, stable	-	-
Hura, 2020 ¹⁴⁷	29	49.8 mean (range 19-91)	14F, 15M	HA, FP, DP, septal deviation	SA, septal deviation, increased fat in PPG fossa	16 R, 10 L, 3 -	FESS, OFR, or none	-	-	-
Manila, 2020 ¹⁴⁸	3	19-69 range	2M, 1 -	-	SA, SO	R	-	-	-	-
Freiser, 2020 ¹⁴⁹	57	12.5 mean (3.7-18 range)	26F, 31M	FP, facial asymmetry	-	-	FESS	RS	-	-
Petraroli, 2020 ¹⁵⁰	1	7	F	HG, facial asymmetry	SA, SO	R	None	Stable	-	-
Le, 2020 ¹⁵¹	1	65	M	DP, change in palpebral sulcus	SO	BL	FESS, OFR	RS	-	-
Bonavolonta, 2020 ¹⁵²	2	35-44	2F	EOT, HG, DP, change in palpebral sulcus, malar depression	SA, SO	2R	FESS, OFR	RS	-	-
Rullan-Oliver, 2020 ¹⁵³	1	47	F	EOT	SA, SO	BL	FESS	RS, later developed contralateral SSS	60	-
AlSaloom, 2020 ¹⁵⁴	1	37	F	Jaw pain, HA	SO	L	FESS	RS	9	none
Leidens, 2020 ¹⁵⁵	1	12	F	EOT, HG	SA, SO	L	FESS	RS	24	none
Farneti, 2020 ¹⁵⁶	1	47	M	EOT, HG, facial asymmetry	SA, SO	BL	FESS	RS, later developed contralateral SSS	60	none
Zheng, 2021 ¹⁵⁶	42	53.6 yo +/- 15.6	19 M, 23 F	Septal deviation	-	25R, 14L, 3BL	FESS	-	-	-
Habib, 2021 ¹⁵⁷	2	33-57 range	1F, 1M	EOT, HG, DP	-	1R, 1-	FESS, OFR	RS	-	-

Study (Author, Year)	n	Age (Years)	Sex	Clinical Presentation	Radiology	Side(s)	Treatments	Outcomes	Fol- low up (months)	Adverse Events
Keren, 2021 ¹⁵⁸	10	16-56 range	7F, 3M	EOT, HA, facial asymmetry, change in palpebral sulcus, infraorbital paresthesia	SA, SO	4R, 6L	FESS	RS	-	-
Ribeiro, 2021 ¹²	1	40	M	HA, post-nasal drip	SO	L	FESS	RS	-	-
Monis, 2021 ¹⁵⁹	1	28	F	EOT, HG, DP	SA, SO	L	FESS	RS	12	none
Deekonda, 2021 ¹⁶⁰	1	54	M	EOT with PMH of CLL	SA, SO	R	FESS	Started ibrutinib for CLL	1	-

Abbreviations: CMA = chronic maxillary atelectasis; PMH = past medical history; CLL = chronic lymphocytic leukemia; Hx = history; CT = computed tomography; SSS = silent sinus syndrome; FESS = functional endoscopic sinus surgery; yo = year old; n/a = not available; EOT = enophthalmos; HG = hypoglobus; DP = diplopia; FP = facial pressure/pain; HA = headache; SA = sinus atelectasis; SO = sinus opacification; CL = Caldwell-Luc; OFR = orbital floor reconstruction; PPG = pterygopalatine ganglion; RS = complete or partial resolution of symptoms; HAG = hyaluronic acid gel.

endoscopic sinus surgery (FESS) involving opening of the osteomeatal complex with a middle meatal antrostomy and/or uncinectomy. Less commonly, septoplasty (n=35) or ethmoidectomy (n=12) was also performed. Eighteen patients underwent a Caldwell-Luc procedure. One hundred patients also received orbital floor reconstruction (typically with an implant), which is offered to patients who are bothered by cosmetic aspects of enophthalmos or hypoglobus, or who have symptomatic diplopia. Twelve patients received intraorbital injection of hyaluronic acid gel rather than surgical orbital floor reconstruction to correct globe position. A minority of patients (n=48) declined FESS or orbital reconstructive surgery or opted for conservative medical treatments such as antibiotics, steroids, or decongestants. Ten of these patients did not receive treatment or surgery of any kind. Of these, outcomes were available for 8 patients. Three of these patients had spontaneous improvement of symptoms, while the others experienced stability of their symptoms. For the remaining patients, three had treatment with prisms or inferior myomectomy for diplopia, but no information was reported on the patients' long-term outcomes regarding SSS symptoms. One patient underwent blepharoplasty for cosmesis, additionally with no further information on SSS disease progression. Case reports for the remaining patients who were treated with medical therapies either did not report on long-term patient results or indicated that the patients had minor symptoms and maintained stability of these symptoms without further progression.

After treatment, patients exhibited significant reductions in enophthalmos (2.67 ± 1.39 vs. 0.33 ± 0.75 mm; $p < 0.001$) and hypoglobus (2.22 ± 1.43 vs. 0.23 ± 0.62 mm; $p < 0.001$). Clinically, most patients (n=263/316) achieved partial or total resolution of their symptoms, with 53 having no symptomatic progression, and no patients experiencing worsening of their disease. In a

minority of patients, there was persistence of minor enophthalmos (n=13), a need for subsequent orbital floor reconstruction to correct persistent diplopia or enophthalmos (n=8), or later presentation with contralateral SSS (n=3). Diplopia improved post-treatment in 32 (86.4%) patients. Follow-up CT results were reported in 44 cases, reporting improved aeration in 35 patients, no change in one patient, and remodeling of one or more maxillary sinus walls in 5 patients. Improved volume of the affected sinus was noted in 21 patients, with a mean increase of 43.8% in volume post-treatment.

Few adverse events (11/146) were reported in connection with treatment of SSS. The most common complication was acute sinusitis (n=3), one of which did not respond to medical therapy and required stent and partial middle turbinectomy. There were two cases of self-resolving hypoesthesia, and seven cases of various ophthalmic conditions including one orbital abscess, persistent enophthalmos, nasolacrimal duct obstruction, lower eyelid retraction, 1 mm of hypoglobus overcorrection, transient diplopia, and transient hypertropia.

Discussion

SSS is an uncommon clinical condition with an incidence rate only currently estimated by published case reports and retrospective studies, highlighting the need for a comprehensive review of the syndrome's presentation, management, and outcomes. On review of the literature, only two other systematic reviews have been conducted on the topic, but they have focused primarily on solidifying a consensus definition of SSS, and only minimally attempted to characterize quantitative and qualitative details on symptomatic presentation, radiographic findings, treatment options, and outcomes^(13,14). In this systematic review and pooled analysis, all 558 cases were analyzed

Table 2. Summary of studies with single subject data (n=213).

Mean age	38.75 years (14.08)
Sex	49.0% female (98 F, 102 M)
Enophthalmos	144/167 (86.2%)
Hypoglobus	106/136 (77.9%)
Diplopia	38/99 (38.4%)
Facial pain/pressure	23/88 (26.1%)
Laterality	89/193 (46.1%) left, 96/193 (49.7%) right, 8/193 (4.1%) bilateral
Adverse events	8/136 (5.9%)
Change in enophthalmos	2.67 (1.39) vs. 0.33 (0.75); p<0.001
Change in hypoglobus	2.22 (1.43) vs. 0.23 (0.62); p<0.001

at a highly granular level to report disaggregated data on these metrics, given that there are no large studies on this rare condition. Other reviews have included at most 55 cases, whereas our review includes all SSS or CMA stage III reports found in the literature and represents the largest of its kind^(13,14).

In this systematic review, we found that a total of 558 cases had been reported across 153 articles. Our results reflect an amalgamation of various reports in the literature, including highest incidence in middle aged adults and with no sex predilection. We found a median age at diagnosis of 39, with a roughly equal distribution between the sexes. Additionally, we found that there does not appear to be a substantial difference in laterality of affected sinus; however, bilateral SSS remains a relatively uncommon but possible clinical presentation.

Treatment of choice for resolving the mechanism of obstruction is FESS to open the osteomeatal complex, with complete uncinectomy, and prevent the reaccumulation of negative intramaxillary pressure. FESS has largely supplanted the Caldwell-Luc approach. Additionally, some patients may experience residual bothersome ophthalmic symptoms, including enophthalmos and hypoglobus or persistent diplopia, and reconstruction of the orbital floor to address these concerns is therefore frequently performed in conjunction or in discontinuity with FESS. We found a statistically significant improvement in both enophthalmos and hypoglobus after treatment, coinciding with our qualitative findings of improved clinical symptoms in over 80% of patients.

Reported adverse events were rare, with severe sinusitis being the most reported. In many cases, the presence or absence of adverse events were not mentioned, suggesting possible underreporting. There were no reports specifically related to orbital

injury during FESS for SSS. Although surgical complication rates vary by surgeon, serious orbital injury has been reported to range from 0.02-6.6% after FESS, though generally less than 1%⁽¹⁶⁻¹⁸⁾. Special care should be taken to avoid these major orbital complications; risk can be mitigated with a thorough preoperative assessment, including imaging to characterize extent of the disease and to pre-identify any anatomic anomalies such as SSS⁽¹⁹⁾.

CMA has been used in the literature interchangeably with SSS, though they are formally differentiated by whether or not sinus-related symptoms are present. Controversy remains over whether the terms should be synonymous or whether the CMA staging system should be universally adopted, due to the significant clinical overlap between CMA stage III and SSS, which have been postulated to be part of the spectrum of the same clinical process^(13,20). CMA was first subdivided by Kass et al. into three stages depending on the progression of maxillary wall atelectasis. CMA stage I (membranous deformity) is defined by lateralization of the maxillary fontanel, stage II (bony deformity) by a progression to inward bowing of at least one osseous wall of the maxillary antrum, and stage III (clinical deformity) by a clinically-apparent enophthalmos, hypoglobus and/or deformity of the midface⁽²¹⁾. Conversely, SSS was first defined by Soparkar and colleagues as a change in the patient's facial appearance, absence of sinusitis, presence of enophthalmos and/or hypoglobus, and CT imaging showing atelectasis of the maxillary sinus⁽²²⁾. Vander Meer et al. further argued for additional exclusion of patients who had experienced orbital trauma or who had a congenital or acquired anatomic abnormality of the sinuses and/or nasal cavities⁽²³⁾. In this review, we thus chose to exclude reports of SSS in patients with prior trauma or surgery, which can present similarly to SSS with enophthalmos due to a damaged orbital floor, though the mechanisms differ. However, the exclusion of post-traumatic SSS in the formal definition is debated. Araslanova and colleagues argued that the radiographic findings of SSS on CT (specifically opacification of the maxillary sinus) are pathognomonic of SSS, and thus traumatic causes of SSS should not preclude its diagnosis in patients with the appropriate symptoms⁽²⁴⁾. Due to the persistent controversy regarding the definition of SSS and the inclusion and exclusion criteria used to describe it, to provide evidence-based, consistent diagnosis and treatment for patients, there is a need for a formalized consensus on the definition and management of the syndrome.

Though care was taken to conduct careful collection and analysis of data, our study has some limitations. Because of the paucity of high-quality evidence published on the subject, analysis was largely relegated to simple descriptive statistics. Additionally, given the rarity of SSS, our review includes a predo-

minance of case reports and case series—with very few larger retrospective and prospective clinical studies—which limits the quality of evidence, granularity of data, and the generalizability of our conclusions.

Conclusion

This systematic review comprehensively reports qualitative and quantitative findings on all published cases of silent sinus syndrome. Though presentation is variable, most patients present with symptoms of enophthalmos and hypoglobus. FESS is an effective treatment to resolve the underlying pathologic process, with synchronous or subsequent orbital reconstruction as an excellent option to correct any residual symptomatic and/or cosmetic orbital defects.

Authorship contribution

Conception and design: ECK. Acquisition of data: LM, ATD. Analysis and interpretation of data: LM, ATD, AA, ECK. Drafting of the manuscript: LM, ATD, AA, ECK. Critical revision of the manuscript: LM, ATD, AA, ECK. All authors approved the final version of the manuscript.

Conflict of interest

The authors report no relevant conflict of interest.

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Edward C. Kuan, MD, MBA
Department of Otolaryngology –
Head and Neck Surgery
University of California Irvine
101 The City Dr South
Orange, CA 92868
USA

Tel: +1-714 456-7017
Fax: +1-714 456-7823
E-mail: eckuan@uci.edu